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Letters to the Editor – Brief papers about basic research or clinical experiences

Gentamicin-based prophylaxis in tunnelled indwelling central venous catheter limbs for haemodialysis do not result in bacterial resistances after a 9 year follow up period☆

La profilaxis con gentamicina de las ramas del catéter venoso central permanente tunelizado en hemodiálisis no causa resistencia bacteriana durante 9 años de evolución

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To the Editor,

Between July 2003 and June 2012, 365 patients received dialysis in our unit. 179 patients had an AV fistula. 186 had a central venous catheter (CVC); of whom 60 were excluded because they had been treated within the previous month with gentamicin (G) for various reasons. Of the 126 patients studied, 118 had a CVC in the internal jugular vein and 8 had it in the femoral vein. Any procedure involving the CVC employed a strict protocol of complete asepsis.[1] *Prophylaxis*: intraluminal post-HD locking with 5 mg Gentamicin (G) + sodium heparin at 1% or 5% per limb. For 6 months, the trough serum level of G was measured (normal value: 0.2–2 μg/mL), subsequently changing to annual controls. If the level was >0.3–0.5 μg/mL, we reduced the lock to 3 mg/limb of G 0.5–2 mg/limb. The diagnosis of CVCB was based on the criteria of Beathard and Urbanes[1] and the NKF guidelines on vascular access published in 2006[2]: clinical improvement in a patient with fever treated with antibiotics with or without removal of CVC, with positive blood cultures (BC+) normally from blood taken from the HD line and/or infrequently from the CVC limb, having excluded other foci of infection. All patients with CVCB had BC+, except one with BC−.

Treatment of CVCB. Gram positive organisms, vancomycin 1 g at the 1st HD and 500 mg at subsequent HDs for 3–4 weeks, or another antibiotics if appropriate; Gram negative, as indicated in the susceptibility testing, for 3–4 weeks. Key outcomes studied: ototoxicity: clinical hypoacusis and/or vertigo. Bacterial resistance to G: organisms normally sensitive to G: Gram+: coagulase negative *Staphylococcus aureus* sensitive to methicillin. Gram−: *Escherichia coli*, *Proteus*, *Serratia*, *Klebsiella*, *Enterobacter*, *Pseudomona aeruginosa*, etc. The minimum inhibitory concentration (MIC) of G for these bacteria is ≤4 μg/mL. Resistance was detected from the results of BCs and susceptibility testing, which expressed sensitivity (S) or resistance (R) to G and the MIC value for each organism. We present the other variables studied in the results section.

Results. The mean patient age was 68 ± 29 years (21–85 years); 60 patients (48%) were women, 39 patients (31%) had diabetes. The mean time each patient remained in the study was 24 months. Thirty-eight patients were treated with prophylaxis for >30 months (30% of all study patients), mean time

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per patient was 50 months (31–108). On susceptibility testing, no resistance was detected in G-sensitive bacteria: the MCI was <4 μg/mL, except in two cases of CVCB due to methicillin-resistant *Staphylococcus aureus*, and one case with BC(−).

No patients had a diagnosis of ototoxicity. The mean trough level of G per patient was 0.17 μg/mL (0.05–0.31). The mean G lock per limb per patient was 3 mg (2–5), equivalent to 1.1–1.7 mg/mL/limb depending on the volume of the limb according to the type of catheter.

Patients diagnosed with CVCB: 11(8.7%). Patients admitted to hospital for CVCB: 4 (3.2%). Number of CVCB/CVC/1000 days: 0.17. CVC removed due to CVCB: 3 patients (2.4%). Mortality due to CVCB: 1 (0.8%). Number of CVCB: 15, *Staphylococcus aureus*: 8; *Staphylococcus epidermidis*: 4; *Escherichia coli*: 1; *Streptococcus bovis*: 1, and BC(−): 1. CVC was removed due to recurrent CVCB in one patient, for failure to improve clinically of in one patient, and due to BC(−) in one patient with clinical remission. There were no other CVCB complications (endocarditis, spondylodiscitis), except in one patient who died due to sepsis.

Discussion. The scientific literature demonstrates that in HD patients, prophylaxis with post-HD antibiotic locking of CVC limbs, including G, reduces morbidity and mortality from bacterial infection associated with CVCB (number of CVCB/CVC/1000 days, mortality and hospital admission due to CVCB) compared with patients with heparin lock alone.[3] Bacterial resistance to G has been reported.[4] However, our experience since July 2003 in patients with CVC attending to the unit and treated with G locking in doses lower than those given in other units (a detail we consider fundamental due to iatrogenic effects), no bacterial resistance or ototoxicity was demonstrated after 9 years of follow-up.[3] Having seen our results, we must refer to the publication by Beathar and Urbanes[1] in which they rate the quality of care of a HD unit according to the number of CVCB/CVC/1000 days it obtains when complete asepsis is employed, an excellent result being a value ≤1. In our case, the practice of complete asepsis + prophylaxis meant that the number of CVCB/CVC/1000 days was 0.17. Although we are unable to compare another study, in 9 years, to obtain a mortality, removal of CVC, and hospital admission due to CVCB of 0.8%, 2.4%, and 3.2%, respectively, is an appreciable standard, obtained thanks to G prophylaxis + universal asepsis. This is further underlined by the absence of endocarditis or spondylodiscitis, except for one patient who died due to sepsis. Strict complete asepsis[5] for all handling procedures of CVC is integral to prophylaxis in reducing morbidity and mortality from bacterial infection associated with CVCB.

Conclusions. This prospective observational study of 9 years' duration in 126 HD patients with a CVC showed: (1) Prophylaxis with intraluminal G locking in CVC limbs does not cause antibiotic resistance in microorganisms sensitive to the antibiotic. (2) There were no diagnoses of clinical ototoxicity, and (3) Prophylaxis with administration of low-dose G (compared with higher doses in other studies)[3] can result in the absence of resistance and ototoxicity.

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The relationship between serum and urine NGAL and graft function in pediatric renal transplant recipients

Relación entre niveles de NGAL en suero y orina y función del injerto en pacientes pediátricos trasplantados renales

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Dear Editor,

We previously serially measured the serum and urine neutrophil gelatinase associated lipocalin (NGAL) during the first